Development and characterization of topical formulations of adefovir dipivoxil for the prevention of HIV infection

Tyler Godinet[1], Abhijit Date[2], Madhur Kulkarni[3]

[1]Department of Tropical Medicine, Medical Microbiology, and Pharmacology,, John A Burns School of Medicine, University of Hawai'i, Honolulu, HI, USA,
[2] The Daniel K. Inouye College of Pharmacy, University of Hawaii Hilo, HI, USA
[3]Department of Pharmaceutics, Indira College of Pharmacy, Pune, MH, India

INTRODUCTION

- HIV infection has been a global health issue for past three decades. Around 2 million new cases of HIV are reported every year, and if left untreated will result in AIDS. Currently, there are no vaccines available to prevent acquisition and transmission of HIV. Majority of HIV infections are acquired through sexual contact. Preventative measures in the form of **Pre-E**xposure **P**rophylaxis (PrEP) have provided an approach to reduce the sexual transmission of the virus.
- Currently, several clinical trials are ongoing to evaluate the efficacy of local (vaginal or rectal) delivery of anti-HIV drugs for reducing sexual transmission of HIV infection.
- Polymeric films are being explored to enable vaginal delivery of anti-HIV drugs for the vaginal PrEP of HIV infections.
- Adefovir dipivoxil (ADV) is an FDA-approved nucleotide reverse transcriptase inhibitor used for the treatment of chronic HBV infections. Studies have shown that ADV is also active against HIV-1 and HIV-2. Thus, it is possible to "repurpose" ADV for the HIV PrEP.

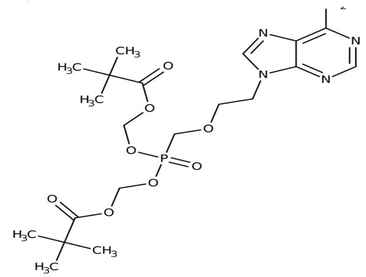
OBJECTIVE

- To develop ADV containing polymeric film to enable repurposing of ADV for the vaginal PrEP of HIV infection

MATERIALS AND METHODS

- **Calibration Curve of ADV in Simulated Vaginal Fluid (SVF)**
  A stock solution of ADV in ethanol was diluted with SVF to obtain solution containing ADV concentration of 4, 8, 16 and 20 ppm respectively. Absorbance of ADV solution was measured at 260.5 nm. Calibration curve was obtained by plotting absorbance versus concentration.
- **Development of Films**
  The placebo films were prepared by solvent casting technique. The solution was poured into a petri plate placed on a flat surface to form a uniform layer and air dried to form a film. The film was then carefully removed and cut into the desired dimensions.
- **Characterization of Films**
  The developed films were tested for organoleptic, physical, and physiochemical properties.
- ***In vitro* release studies**
  In vitro release of ADV from polymeric films was studied using a Franz diffusion cell. Aliquots were taken at 30, 60, 120, 180, 240, 300, and 360 min and the amount of ADV released was calculated by measuring the absorbance.

Adefovir Dipivoxil Structure



"Repurposing" and reformulating hepatitis B virus medication for prevention of sexual transmission of HIV

godinett@hawaii.edu

RESULTS

The films prepared with HPMC K100LV (3%) and PVP K30 (1%) as well as the ones with HPMC K100 LV (3%) and ethyl cellulose 7 cps (0.5%) showed acceptable organoleptic and physical properties.

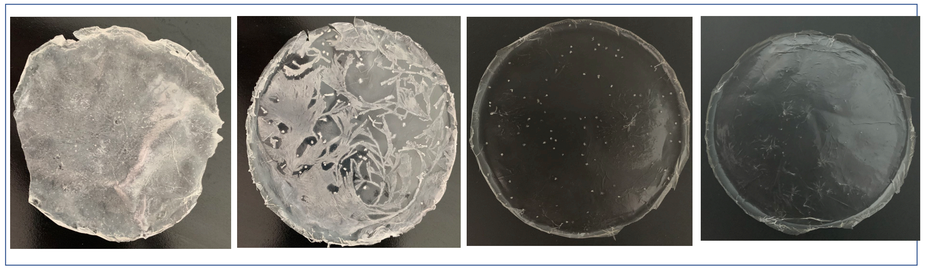


Figure 1. The optimization of content of ADV in the polymeric films. ADV content/unit surface area from right to left: 10 mg/4 cm^2, 8 mg/4.5 cm^2, 5 mg/4.5 cm^2, 5 mg/7.5 cm^2. The quantity of ADV/unit surface area showed significant impact on the appearance and physical properties of the film.

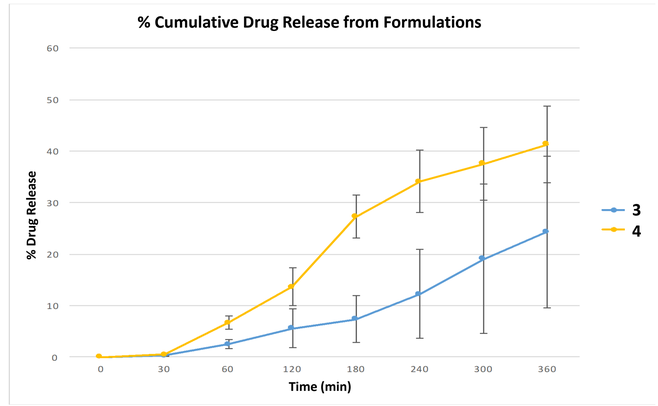


Figure 2. *In vitro* release studies using Franz diffusion cell showed that the composition of the film had an impact on the release of ADV from the film.

CONCLUSIONS

- Vaginal films impregnated with ADV films may be used as a vaginal microbicide product that could effectively provide pre-exposure prophylaxis against sexual transmission of HIV.

ACKNOWLEDGEMENTS

We thank Akshay S., Ankita B., Tejashree G. for their assistance in the laboratory and Dr. Vivek R. Nerurkar, Dr. Angela Sy, Keeton Krause for giving us this opportunity to conduct research in Pune, India. We thank Indira College of Pharmacy Pune, India, and staff for their assistance throughout this project. This research was supported by the Minority Health International Research Training (MHIRT) Program at the University of Hawaii through the NIMHD, National Institutes of Health (NIH) grant (T37MD008636-05). We acknowledge the support of UH Pacific Center for Emerging Infectious Diseases Research, COBRE funded through the NIGMS, NIH grant (P30GM114737).